PRESCRIBING IN NORTHERN IRELAND
STUDY No. 2
SYSTEMATIC ANTI-INFECTIVES

by

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THE public and the medical profession generally regard the "antibiotics", by which they mean the synthetic anti-infectives as well as those produced by micro-organisms, as the most beneficial group of drugs introduced in the last 35 years. Some concern has been expressed from time to time about the ways they are used, especially in hospital and as an additive to animal feed stufis. But on the whole the effects of their use are thought to be beneficial. The mortality rate from some infections has fallen dramatically and the pattern of infectious diseases in the community has changed. If this has been an improvement, then the need to prescribe anti-infectives should dwindle. The following study of prescribing was prompted by the knowledge that the prescribing has not dwindled. It was not expected that the study would explain why the prescribing of anti-infectives is still rising, but it was hoped that the results would stimulate further research into the benefits and dangers.

METHODS

Using the technique described in the preliminary paper (Elmes, Hood and Wade, 1976), the prescribing of anti-infectives by all practitioners has been recorded and analysed. To this has been added information about the purchasing of anti-infectives for hospital use so that the total consumption in Northern Ireland can be compared with that of Finland, Norway and Sweden. The prescribing figures have been available here since 1966 and have been used to assess both the total quantity of prescribing and the changes in quantity and choice of drugs which has occurred during the ten-year period. As in the previous report, the information is given in the form of defined daily doses (DDD) per 1,000 of the population per day. The defined daily doses of the important (frequently prescribed) preparations are given in Table 1. These are adult doses and if the preparation is only used for adults it will give an estimate of the number of patients/1,000 of the population on that preparation. Much antibiotic prescribing is for children when the daily dose is usually less than the adult dose. In this

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TABLE 1: DEFINED DAILY DOSES (DDD) OF FREQUENTLY PRESCRIBED ANTIBACTERIAL PREPARATIONS

Approved Name	*Proprietary Names*	*DDD*
1. TETRACYCLINES		
Demethylchlortetracycline	Ledermycin	0.6g
Oxytetracycline	Imperacin	1g
Tetracycline	Achromycin	1g
	Tetracycline	1g
2. CHLORAMPHENICOL	Chloromycetin	3g
3. AMPICILLINS	Penbritin	2g
	Magnapen	
4. CEPHALOSPORINS	Ceporex	1.5g
	Keflex	
5. CO-TRIMOXATOLE	Bactrim	4 tabl.
	Septrin	4 tabl.
6. PENICILLINS		
Phenoxymethyl penicillin	Crystapan V	
	Distaquaine V	900mgm
	Penicillin V	
	V. Cil K.	
Propicillin	Brocillin	
	Ultrapen	0.45g
7. CLINDAMYCIN	Dalacin C	0.6g
8. LINCOMYCIN	Lincocin	1.5g

instance, the number of daily doses (DDD) per 1,000/day will underestimate the number of patients receiving that treatment. Especially in children, courses of antibiotics are not often completed, the surplus tablets being thrown away, or kept in the bathroom cabinet for a future occasion. This lack of "compliance" by the patient means that the prescribed DDD/1,000/day overestimates the actual consumption. These two errors are intrinsic in the method and are the subject of further investigation.

FINDINGS

The total consumption of systemic antibiotics was 6.6 daily doses per 1,000/day in 1966 and has risen linearly to exactly twice that in ten years (see Fig. 1). During the first five years this increase was due to a parallel increase in the three most popular types of preparation. These were the tetracyclines, which rose from 3 to 4.3 DDD/1,000/day; the oral penicillins (other than ampicillin), from 2.4 to 3.1 DDD/1,000/day; and ampicillin, which rose from 0.8 to 1.8 DDD/1,000/day. However, co-trimoxazole (Bactrim and Septrin) had been introduced during this period and by 1970 0.9 DDD/1,000/day were being prescribed. From 1970 onwards the increase in prescribing of co-trimoxazole and ampicillin continued, but the prescribing of the other penicillins and of the tetracyclines both fell a little. Two preparations of co-trimoxazole had been marketed at the same time as a result of combined research by two drug companies and were known to be

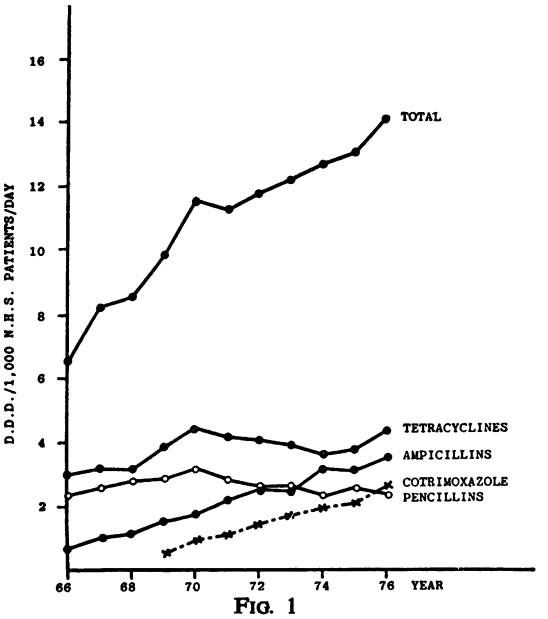

FIG. 1

therapeutically identical. The prescribing of the two has diverged markedly since 1972 (see Fig. 2). As there is no cost difference, some other commercial pressure had led to this divergence.

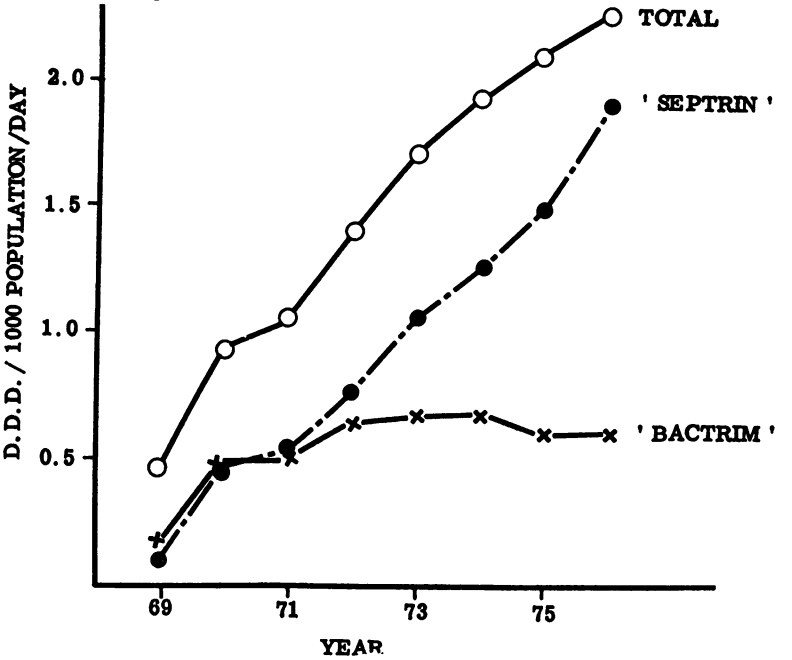

FIG. 2

SEASONAL VARIATIONS

Figure 3 shows a monthly analysis of all the total anti-infective prescribing for 1975. As expected, the peak of prescribing occurred in the winter months of December, January and February, and the trough appeared in the summer months of June, July and August. This pattern was paralleled by each of the sub-groups and is particularly noticeable with the frequently-used preparations.

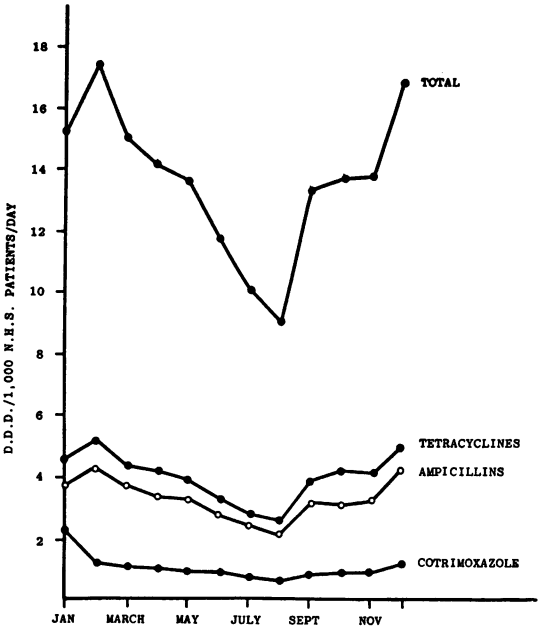

FIG. 3

GEOGRAPHICAL VARIATIONS WITHIN NORTHERN IRELAND

Table 2 compares the prescribing levels for each of the new area boards, dividing the more heavily populated Eastern Board into two (E1, Belfast City;

TABLE 2: THE TOTAL ANTI-INFECTIVE PRESCRIBING RATE FOR EACH AREA BOARD FROM 1974 TO 1976 EXPRESSED AS DDD/1,000 POPULATION/DAY

	1974	-	1975	-	1976
Eastern Board 1	12.76	-	13.57	-	13.87
Eastern Board 2	11.86	-	12.33	-	13.73
Northern Board	12.09	-	12.84	-	13.65
Southern Board	13.47	-	13.94	-	14.61
Western Board	12.27	-	11.73	-	15.56

E2, rest) for the years 1974-5-6. Fig. 4 Shows a map of the distribution for 1976. When such a geographical analysis is carried out for all drugs a higher level of prescribing is found in the densely populated areas (Belfast itself and the rest of the Eastern area). The geographical differences are particularly marked for psychotropic drugs, which are nearly twice as frequently prescribed in the Belfast area as in rural County Londonderry (Elmes, Hood, McMeekin and Wade, 1976). However, for anti-infective drugs the level of prescribing is more uniform, the coefficient of variance being 5 per cent in 1974 and 6 per cent in 1975.

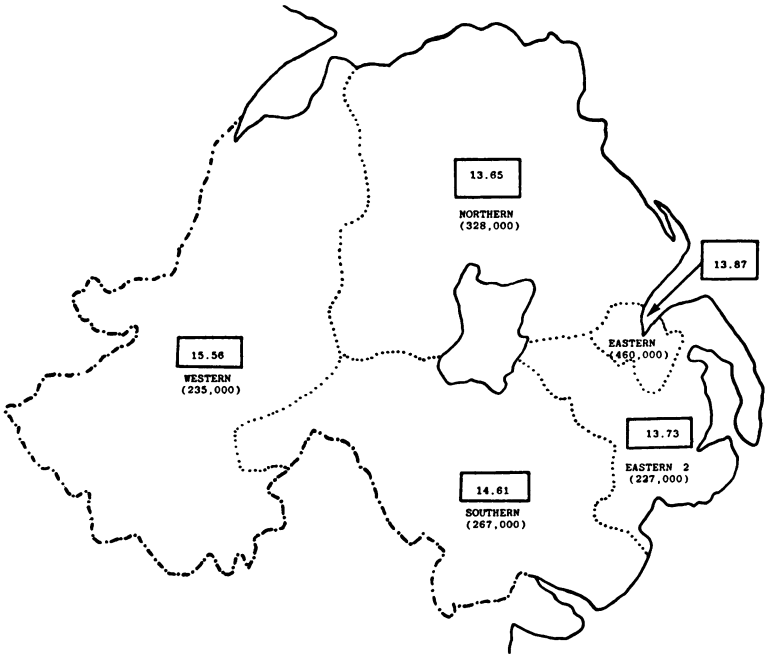

FIG. 4

Prescribing in the Belfast area (Eastern 1) and County Down (Eastern 2) is relatively low in all three years.

On comparing the prescribing of the main antibiotic groups, greater differences between the area boards become apparent (see Fig. 5). For instance, in the Southern Area the prescribing of antibiotics is the same as the average for the Province, except for the high prescribing of co-trimoxazole in the form of Septrin. But statistical analysis indicates that these differences are due to random variation.

GEOGRAPHICAL COMPARISON WITH NORWAY AND SWEDEN

Complete information has not been available for sufficiently long to make reliable comparisons, but the overall trend is for increasing use. Total prescribing is highest for all drugs in Sweden and this also applies to anti-infectives. The

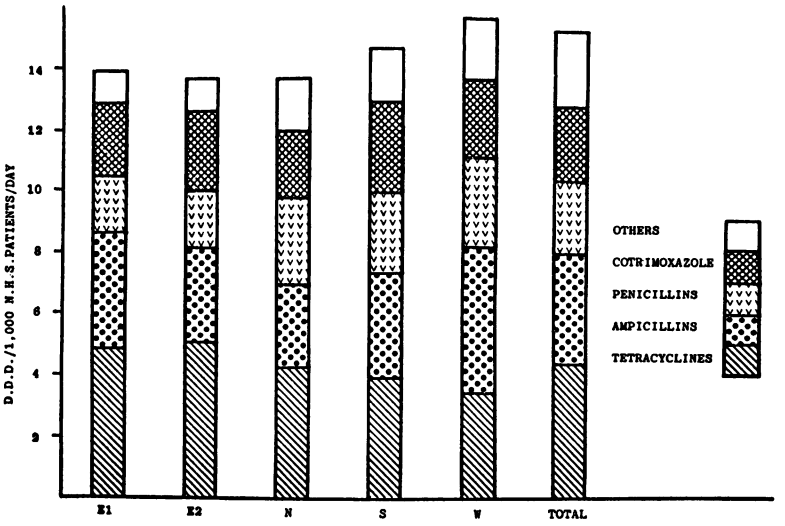

FIG. 5

prescribing there was over 16 DDD/1,000/day in 1975 when in Northern Ireland it was just over 13 DDD/1,000/day and Norway had not reached 10 DDD/1,000/day in 1974. Fig. 6 shows the information available. The ampicillins (Penbritin

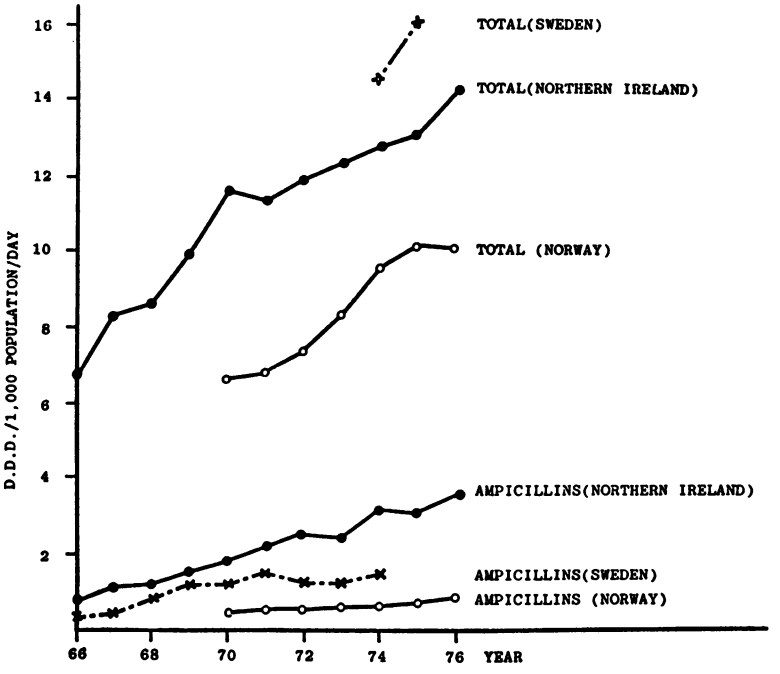

FIG. 6

and Magnapen) have been prescribed increasingly frequently in all three countries but remain relatively unpopular in Scandinavia. These broad spectrum penicillins accounted for 8 per cent and 10 per cent of the antibiotic prescribing in Norway and Sweden respectively at a time when they formed 22 per cent of the antibiotic prescribing in Northern Ireland.

THE PRESCRIBING OF OTHER ANTIBIOTICS IN NORTHERN IRELAND

In 1976 prescribing of the cephalosporins at 0.62/DDD/1,000/day was higher than that of erythromycin (0.50 DDD) for the first time. Up until then erythromycin was the more frequently prescribed of these two which are promoted for treating respiratory and other common infections. The other antibiotics (chloramphenalcol, lincomycin, clindamycin and streptomycin) should only be used in special circumstances.

In tracing the changes in level of prescribing in the last 10 years, it is noticeable that chloramphenicol has fallen from 0.06 to a negligible quantity. Streptomycin has fallen from 0.15 to 0.03. In both cases their use should be limited to the management of relatively uncommon infections.

ROUTE OF ADMINISTRATION

Nearly 80 per cent of anti-infective prescribing is for tablets or capsules. Although liquid oral preparations are available for the very old or very young, they only account for as much as a third of the prescribing in the case of co-trimoxazole.

These figures include hospital prescribing and the stock prescriptions used by general practitioners to replenish their supply of ampoules for immediate use. Even so, antibiotics by injection are a trivial part of the total. Gentamycin (when not in topical preparations) is used entirely by injection, but even in hospitals the total usage is also trivial (Table 3).

TABLE 3: BREAKDOWN OF MAIN PREPARATION ACCORDING TO ROUTE OF ADMINISTRATION 1975

	Tablet or Capsule	*Oral Liquid*	*Injection*
Penicillin	1.45	0.51	0.02
Ampicillin	2.20	0.71	—
Tetracyclines	3.52	0.22	—
Co-Trimoxazole	1.51 (0.14)	0.58 (0.04)	—
Cephalosporins	0.35 (0.01)	0.11	— (0.01)
Erythromycin	0.31	0.28	—
Streptomycin	0.02	0.01	—
Gentamycin	—	—	— (—)
Lincomycin	0.05	0.01	—
	9.56 (79%)	2.47 (20%)	0.03 (1%)

Examples of hospital prescribing are given in brackets and form a trivial part of the whole.
"—" = less than 0.01 DDD/1,000/Day.

The topical use of antibiotics is not included in this analysis as it is the subject of a separate study.

DISCUSSION

This analysis reveals a steady increase in the prescribing of anti-infectives but does not indicate whether this is related to a rise in the incidence of clinical bacterial infections. Analysis of the indications for prescribing would be necessary to establish this. Whether they are administered to treat established bacterial infections or to prevent them, their increasing use can be justified if the morbidity and mortality due to bacterial infections in the community is seen to be reduced.

Such beneficial effects are difficult to measure with existing information. Morbidity (sickness absence) information is recorded but not in sufficient detail. Deaths are recorded in more detail. Deaths from tuberculosis have continued to fall during the past ten years. The bulk of the anti-infective prescribing is for "other infections". Among these are ICD Nos. 030-039, which in Northern Ireland have remained constant between 1968 and 1976. Within this group death due to whooping cough and tetanus (which are prevented by vaccination) have fallen from four each year to nil. In contrast, septicaemia deaths have risen by 30 per cent. Numerically more important in Northern Ireland are deaths from pneumonia (ICD 480-486). These have risen from 687 in 1968 to 804 in 1976. Viral pneumonia has remained constant and there has been a 20 per cent increase in death due to pneumococcal infections as well as to bronchopneumonia.

Antibiotics carry a relatively high risk of adverse reactions and regularly occupy the first few places in national and international reporting systems for adverse reactions. Hospital monitoring studies in Belfast indicated in 1965-66 that the most frequently used antibiotic (ampicillin) produced an adverse reaction in 7.8 per cent of patients (Hurwitz and Wade, 1969). A follow-up in the same hospital in 1975 showed co-trimoxazole to be the most frequently administered preparation and it produced adverse reactions in 3.4 per cent of patients. Side effects in patients treated at home are frequent but minor and they are not a frequent cause of admission to hospital.

There is an indirect side effect of antibiotic usage which has led to restrictions being placed on their addition to animal foodstuffs following the report of the Swann Committee (Swann, 1969). Hospitals have also had to adopt antibiotic policies to control their use. When antibiotics are present in an environment, a change in the bacterial flora occurs with the replacement of sensitive organisms by ones which are resistant. Infections arising in such an environment are increasingly likely to be due to these resistant organisms and to require treatment with newly-introduced antibacterial agents. These changes occur relatively slowly outside hospital, but already the usefulness of benzyl penicillin, ampicillin and tetracyclines and the sulphonamides for the treatment of common infections arising at home has been seriously impaired. Failure to respond to treatment can be regarded as a negative side effect of previous antibiotic use. These considerations do not appear to have influenced the prescribing of antibiotics in Northern Ireland during the last 10 years. If certain infections are now resistant to benzyl penicillin

and ampicillin, you would have expected their use to have diminished rapidly and their replacement by flucloxacillin and co-trimoxazole respectively. Although the prescribing of these last two has risen, that of benzyl penicillin and the related oral penicillins has hardly fallen and the use of the ampicillins continues to increase.

Many of the positive side effects of antibiotic therapy are due to immediate or delayed allergies. Given to a population not previously exposed, the frequency and severity of these effects is low. But as the number of patients given the drug rises, so that likelihood of a sensitised patient receiving a further course of treatment and developing serious allergy or anaphylaxis increases. This is occurring with both penicillins where the situation seems reasonably stable and acceptable, and with co-trimoxazole where the incidence of serious allergy to the sulphonamide component may still be increasing.

SUMMARY

Analysis of the Northern Ireland prescribing, both in hospital and at home, shows the increased use of drugs for bacterial infections. The overall rise of 10 per cent a year is due to an even greater increase in prescribing of popular broad spectrum agents (ampicillin and co-trimoxazole). The prescribing pattern and the increase shows no geographical variation within the Province. Allowing for different initial levels of prescribing, the same pattern of change is seen in Norway and Sweden. These drugs frequently cause adverse reactions. Evidence of benefit is hard to obtain and the death rate from some of the relevant infections has increased.

ACKNOWLEDGMENTS

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